pyogenes because bacterial species will be more similar to each other than to mammals. Extensive comparisons of IMPDH structure among bacteria and between mammals are disclosed. (Table 2)

On page 8-9, methods are disclosed for determining bacterial IMPDH crystal structure. A map shows a "clearly defined electron density for the IMPDH substrate, bound in the catalytic site," (page 9, lines 22-24). Based on this invention, a model is now available for bacterial IMPDH which provides a framework on which differences among bacteria may be sought.

III. Summary of the Interview of January 15, 2004: Enablement, Written Description

Applicant appreciates Primary Examiner Marschel's comments during the telephone interview of January 15, 2004 with applicant's representative, Alice O. Martin, and an inventor, Dr. Collart.

The prosecution history since the filing date March 23, 2000 was reviewed. Applicants hoped to resolve confusions due to different positions taken by the different examiner's involved in the prosecution.

Dr. Marschel identified one possible source of confusion - whether there was a single species of the IMPDH with a single amino acid sequence, or whether there were multiple species.

In response, Dr. Collart explained that although there are small amino acid sequence differences, the enzyme from a similar organism or the same species, is not highly variant. The overall protein shape (protein fold) is expected to be similar for all bacteria. By definition, all IMPDH enzymes must bind IMP at a specific site defined as the binding pocket. The specification describes an IMPDH protein with IMP localized in the binding site. Furthermore, the inventors describe specific molecular contacts between IMP and the specific amino acids in the protein. Substitution of the contact atoms on IMP is a step for the design of inhibitors. Of course, those skilled in the art could apply more sophisticated methods for drug discovery using the information provided by the structure. Citations to the literature are in the record as evidence that those of skill in the art could design lead compounds based on the present disclosure.

The technique of molecular replacement is well known to those skilled in the art and can be used obtaining initial phasing for an unknown structure from a known, structurally related molecule (J.P. Turkenburg and E.J. Dodson Modern developments in molecular replacement. *Curr. Opin. Struct. Biol.* 1996 Oct;6(5):604-10). When there is a certain level of sequence homology, and the coordinates of the binding pocket of the species is known, 3-D structure is expected to be similar, and an inhibitor that works in the first species is a lead candidate for a inhibitor in a related species. Therefore, Dr. Collart is entitled to claim scope for developing lead compounds in bacteria, not just in *S. pyogenes.*

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